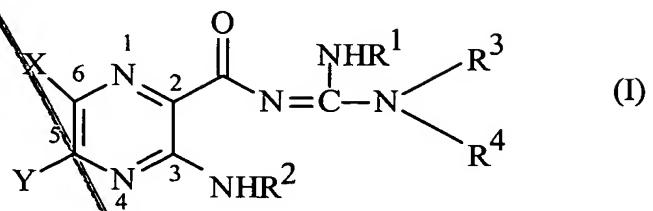


CLAIMS:

1. A compound represented by formula (I):



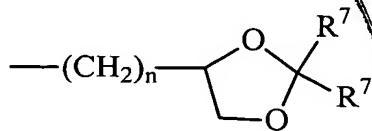
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or $-N(R^2)_2$;

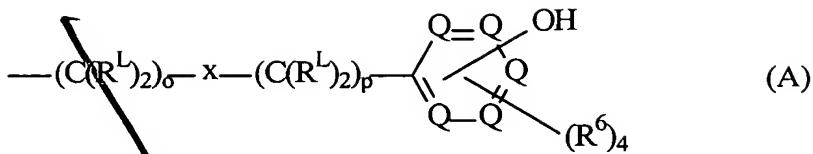
R^1 is hydrogen or lower alkyl;

each R^2 is, independently, $-R^7$, $-(CH_2)_m-OR^8$, $-(CH_2)_m-NR^7R^{10}$, $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2CH_2O)_m-R^8$, $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$, $-(CH_2)_n-C(=O)NR^7R^{10}$, $-(CH_2)_n-Z_g-R^7$, $-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$, $-(CH_2)_n-CO_2R^7$, or



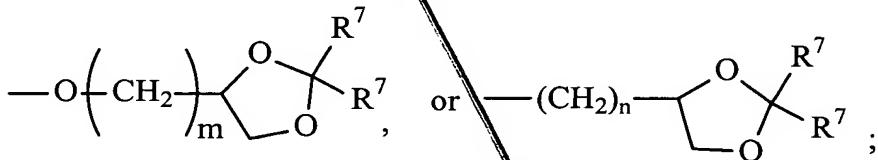
15 R^3 and R^4 are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of R^3 and R^4 is a group represented by formula (A):

a'
cont



wherein

each R^{L} is, independently, $-\text{R}^7$, $-(\text{CH}_2)_n\text{---OR}^8$, $-\text{O}-(\text{CH}_2)_m\text{---OR}^8$,
 $-(\text{CH}_2)_n\text{---NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m\text{---NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n\text{---CH}_2\text{OR}^8$,
 $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n\text{---CH}_2\text{OR}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m\text{---R}^8$,
 $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m\text{---R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m\text{---CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$,
 $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m\text{---CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n\text{---C(=O)\text{NR}^7\text{R}^{10}}$,
 $-\text{O}-(\text{CH}_2)_m\text{---C(=O)\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n\text{---(Z)}_g\text{---R}^7$, $-\text{O}-(\text{CH}_2)_m\text{---(Z)}_g\text{---R}^7$,
 $-(\text{CH}_2)_n\text{---NR}^{10}\text{---CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n\text{---CH}_2\text{OR}^8$,
 $-\text{O}-(\text{CH}_2)_m\text{---NR}^{10}\text{---CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n\text{---CH}_2\text{OR}^8$,
 $-(\text{CH}_2)_n\text{---CO}_2\text{R}^7$, $-\text{O}-(\text{CH}_2)_m\text{---CO}_2\text{R}^7$, $-\text{OSO}_3\text{H}$, $-\text{O}\text{-glucuronide}$, $-\text{O}\text{-glucose}$, or



each x is, independently, O , NR^7 , C=O , CHOH , C=N-R^6 , or represents a single bond;

each o is, independently, an integer from 0 to 10;

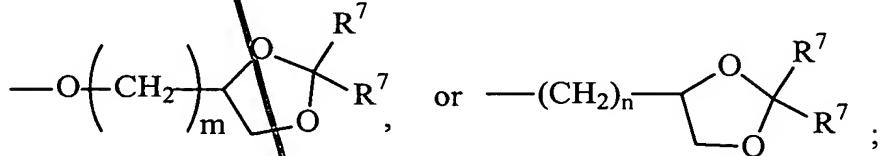
each p is, independently, an integer from 0 to 10;

15 with the proviso that (a) the sum of o and p in each contiguous chain is from 1 to 10 when x is O , NR^7 , C=O , or C=N-R^6 or (b) that the sum of o and p in each contiguous chain is from 4 to 10 when x represents a single bond;

each R^6 is, independently, $-\text{R}^7$, $-\text{OH}$, $-\text{OR}^{11}$, $-\text{N}(\text{R}^7)_2$, $-(\text{CH}_2)_m\text{---OR}^8$,
 $-\text{O}-(\text{CH}_2)_m\text{---OR}^8$, $-(\text{CH}_2)_n\text{---NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m\text{---NR}^7\text{R}^{10}$,
 $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n\text{---CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_n\text{---CH}_2\text{OR}^8$,
 $-(\text{CH}_2\text{CH}_2\text{O})_m\text{---R}^8$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m\text{---R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m\text{---CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$,
 $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m\text{---CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n\text{---C(=O)\text{NR}^7\text{R}^{10}}$,

$-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}, -(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7, -\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7,$
 $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8,$
 $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8,$
 $-(\text{CH}_2)_n-\text{CO}_2\text{R}^7, -\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7, -\text{OSO}_3\text{H}, -\text{O}-\text{glucuronide}, -\text{O}-\text{glucose},$

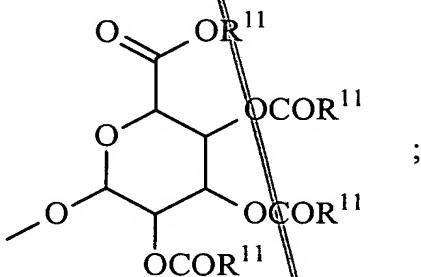
cont



5 wherein when two R^6 are $-\text{OR}^{11}$ and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two R^6 may be bonded together to form a methylenedioxy group;

each R^7 is, independently, hydrogen or lower alkyl;

each R^8 is, independently, hydrogen, lower alkyl, $-\text{C}(=\text{O})-\text{R}^{11}$, glucuronide, 2-tetrahydropyranyl, or



each R^9 is, independently, $-\text{CO}_2\text{R}^7, -\text{CON}(\text{R}^7)_2, -\text{SO}_2\text{CH}_3$, or $-\text{C}(=\text{O})\text{R}^7$;

each R^{10} is, independently, $-\text{H}, -\text{SO}_2\text{CH}_3, -\text{CO}_2\text{R}^7, -\text{C}(=\text{O})\text{NR}^7\text{R}^9,$

$-\text{C}(=\text{O})\text{R}^7$, or $-\text{CH}_2-(\text{CHOH})_n-\text{CH}_2\text{OH}$;

each Z is, independently, $\text{CHOH}, \text{C}(=\text{O}), \text{CHNR}^7\text{R}^{10}, \text{C}=\text{NR}^{10}$, or NR^{10} ;

each R^{11} is, independently, lower alkyl;

each g is, independently, an integer from 1 to 6;

each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

20 each Q is, independently, $\text{C}-\text{R}^5, \text{C}-\text{R}^6$, or a nitrogen atom, wherein at most three Q in a ring are nitrogen atoms;

or a pharmaceutically acceptable salt thereof, and
inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

*a¹
Cont*

2. The compound of Claim 1, wherein Y is -NH₂.

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3. The compound of Claim 2, wherein R² is hydrogen.

4. The compound of Claim 3, wherein R¹ is hydrogen.

5. The compound of Claim 4, wherein X is chlorine.

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6. The compound of Claim 5, wherein R³ is hydrogen.

7. The compound of Claim 6, wherein each R^L is hydrogen.

8. The compound of Claim 7, wherein o is 4.

9. The compound of Claim 8, wherein p is 0.

10. The compound of Claim 9, wherein x represents a single bond.

11. The compound of Claim 10, wherein each R⁶ is hydrogen.

15

12. The compound of Claim 11, wherein at most one Q is a nitrogen atom.

13. The compound of Claim 12, wherein no Q is a nitrogen atom.

14. The compound of Claim 1, wherein
X is halogen;
Y is -N(R⁷)₂;

20

R¹ is hydrogen or C₁-C₃ alkyl; and
R² is -R⁷, -(CH₂)_m-OR⁷, or -(CH₂)_n-CO₂R⁷;

*A¹
cont*

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R^3 is a group represented by formula (A); and
 R^4 is hydrogen, a group represented by formula (A), or lower alkyl;

15. The compound of Claim 14, wherein

X is chloro or bromo;

Y is $-N(R^7)_2$;

R^2 is hydrogen or C_1 - C_3 alkyl;

at most three R^6 are other than hydrogen as defined above;

at most three R^L are other than hydrogen as defined above; and

at most 2 Q are nitrogen atoms.

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16. The compound of Claim 15, wherein Y is $-NH_2$.

17. The compound of Claim 16, wherein

R^4 is hydrogen;

at most one R^L is other than hydrogen as defined above;

at most two R^6 are other than hydrogen as defined above; and

at most 1 Q is a nitrogen atom.

18. The compound of Claim 17, wherein x is O , NR^7 , $C=O$, $CHOH$, or $C=N-R^6$.

19. The compound of Claim 17, wherein x represents a single bond.

20. The compound of Claim 1, wherein x is O , NR^7 , $C=O$, $CHOH$, or $C=N-R^6$.

21. The compound of Claim 1, wherein x represents a single bond.

20

22. The compound of Claim 1, wherein each R^6 is hydrogen.

23. The compound of Claim 1, wherein at most two R^6 are other than hydrogen as defined in Claim 1.

24. The compound of Claim 1, wherein one R⁶ is other than hydrogen as defined in Claim 1.

25. The compound of Claim 1, wherein one R⁶ is -OH.

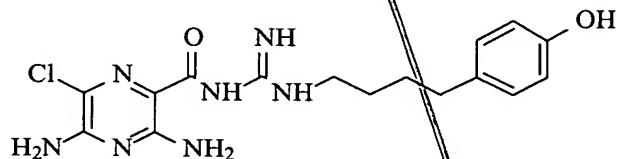
26. The compound of Claim 1, wherein each R^L is hydrogen.

5 27. The compound of Claim 1, wherein at most two R^L are other than hydrogen as defined in Claim 1.

10 28. The compound of Claim 1, wherein one R^L is other than hydrogen as defined in Claim 1.

29. The compound of Claim 1, wherein x represents a single bond and the sum of o and p is 4 to 6.

30. The compound of Claim 1, which is represented by the formula

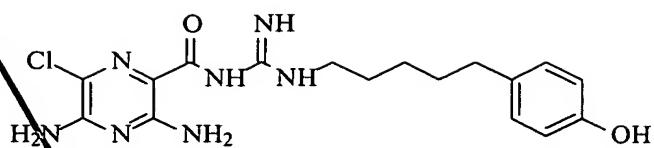


31. The compound of Claim 30, which is in the form of a pharmaceutically acceptable salt.

32. The compound of Claim 31, which is in the form of a hydrochloride salt.

15 33. The compound of Claim 1, which is represented by the formula

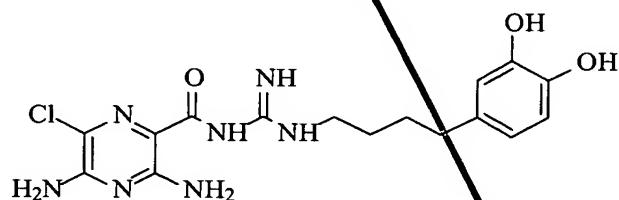
*Q1
cont*



34. The compound of Claim 33, which is in the form of a pharmaceutically acceptable salt.

35. The compound of Claim 34, which is in the form of a hydrochloride salt.

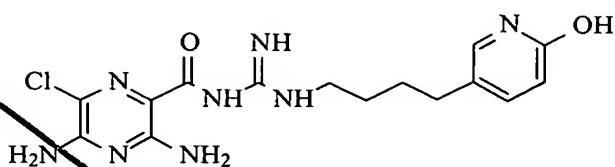
36. The compound of Claim 1, which is represented by the formula



5 37. The compound of Claim 36, which is in the form of a pharmaceutically acceptable salt.

38. The compound of Claim 37, which is in the form of a hydrochloride salt.

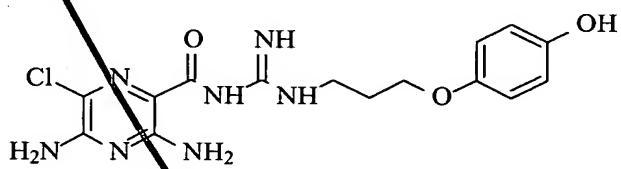
39. The compound of Claim 1, which is represented by the formula



40. The compound of Claim 39, which is in the form of a pharmaceutically acceptable salt.

41. The compound of Claim 40, which is in the form of a hydrochloride salt.

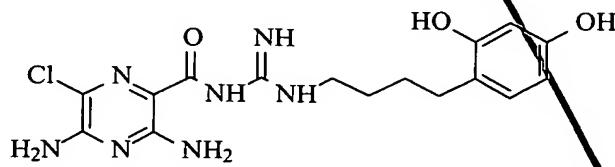
42. The compound of Claim 1, which is represented by the formula



5 43. The compound of Claim 42, which is in the form of a pharmaceutically acceptable salt.

44. The compound of Claim 43, which is in the form of a hydrochloride salt.

45. The compound of Claim 1, which is represented by the formula



46. The compound of Claim 45, which is in the form of a pharmaceutically acceptable salt.

47. The compound of Claim 46, which is in the form of a hydrochloride salt.

5 48. The compound of Claim 1, which is in the form of a pharmaceutically acceptable salt.

49. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

10 50. A method of promoting hydration of mucosal surfaces, comprising: administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

51. A method of restoring mucosal defense, comprising: topically administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject in need thereof.

15 52. A method of blocking sodium channels, comprising: contacting sodium channels with an effective amount of the compound of Claim 1.

53. A method of treating chronic bronchitis, comprising: administering an effective amount of the compound of Claim 1 to a subject in need thereof.

20 54. A method of treating cystic fibrosis, comprising: administering an effective amount of the compound of Claim 1 to a subject in need thereof.

55. A method of treating sinusitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

*Q1
cont*
56. A method of treating vaginal dryness, comprising:
administering an effective amount of the compound of Claim 1 to the vaginal tract of a
subject in need thereof.

57. A method of treating dry eye, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject
in need thereof.

10 58. A method of promoting ocular hydration, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject.

59. A method of promoting corneal hydration, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject.

150 60. A method of promoting mucus clearance in mucosal surfaces, comprising:
administering an effective amount of the compound of Claim 1 to a mucosal surface of
a subject.

61. A method of treating Sjogren's disease, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

20 62. A method of treating distal intestinal obstruction syndrome, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

*Q
out*

63. A method of treating dry skin, comprising:
administering an effective amount of the compound of Claim 1 to the skin of a subject
in need thereof.

5 64. A method of treating esophagitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

10 65. A method of treating dry mouth (xerostomia), comprising:
administering an effective amount of the compound of Claim 1 to the mouth of a
subject in need thereof.

150 66. A method of treating nasal dehydration, comprising:
administering an effective amount of the compound of Claim 1 to the nasal passages
of a subject in need thereof.

15 67. The method of Claim 66, wherein the nasal dehydration is brought on by
administering dry oxygen to the subject.

150 68. A method of preventing ventilator-induced pneumonia, comprising:
administering an effective amount of the compound of Claim 1 to a subject on a
ventilator.

20 69. A method of treating asthma, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

70. A method of treating primary ciliary dyskinesia, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

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Cont
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71. A method of treating otitis media, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

72. A method of inducing sputum for diagnostic purposes, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

73. A method of treating chronic obstructive pulmonary disease, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

74. A method of treating emphysema, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

75. A method of treating pneumonia, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

76. A method of treating constipation, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

77. The method of Claim 76, wherein the compound is administered orally or via a
suppository or enema.

78. A method of treating chronic diverticulitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

79. The present invention also provides a method of treating rhinosinusitis, comprising:

administering an effective amount of the compound of Claim 1 to a subject in need thereof.

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80. A composition, comprising:
the compound of Claim 1, and
a P2Y2 inhibitor.

81. A composition, comprising:
the compound of Claim 1; and
a bronchodilator.